JUN - 5 2012

510(k) Summary

Introduction

According to the requirements of 21 CFR 807.92, the following provides sufficient detail to understand the basis for a determination of substantial equivalence.

Submitter, name, address, contact

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Date prepared: June 1, 2012

Device name

Assay:
Proprietary name: Homocysteine Enzymatic Assay
Common name: Homocysteine test system
Classification name: Urinary homocystine (nonquantitative) test system under 21 CFR 862.1377
Product code: LPS

Calibrator:
Proprietary name: Homocysteine Calibrator Kit
Common name: Calibrator
Classification name: 21 CFR 862.1150
Product code: JIX

Control:
Proprietary name: Homocysteine Control Kit
Common name: Quality control material (assayed and unassayed)
Classification name: 21 CFR 862.1660
Product code: JJX

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510(k) Summary, Continued

Device description

Assay:
The Homocysteine Enzymatic Assay is based on an enzyme cycling assay principle that assesses the co-substrate conversion product. In this assay, oxidized homocysteine (Hcy) is first reduced to free Hcy which then reacts with a co-substrate, S-adenosylmethionine, to form methionine and S-adenosylhomocysteine (SAH), catalyzed by a Hcy S-methyltransferase. SAH is assessed by coupled enzyme reactions where SAH is hydrolyzed into adenosine (Ado) and Hcy by SAH hydrolase, and Hcy is cycled into the Hcy conversion reaction to form a reaction cycle that amplifies the detection signal. The formed Ado is immediately hydrolyzed into inosine and ammonia which reacts with glutamate dehydrogenase with concomitant conversions of NADH to NAD^+. The concentration of Hcy in the sample is indirectly proportional to the amount of NADH converted to NAD^+ which is measured spectrophotometrically at 340 nm.

Calibrator:
The Homocysteine Calibrator Kit is a liquid, ready-for-use calibrator based on human serum. It is a single level calibrator with lot specific values and diluted on board the analyzer to create a 5-point calibration curve.

Control:
The Homocysteine Control Kit consists of two ready-for-use controls based on human serum. The adjusted concentrations of the control components are in the low range for Control 1 and in the elevated range for Control 2.

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Intended use

Assay:
The Homocysteine Enzymatic Assay is an in vitro test for the quantitative determination of total L-homocysteine in human serum and plasma on Roche/Hitachi **cobas c** systems. The assay can assist in the diagnosis of patients suspected of having hyperhomocysteinemia or homocystinuria.

Calibrator:
The Homocysteine Calibrator Kit is intended for use in the calibration of quantitative Roche methods on Roche clinical chemistry analyzers as specified in the value sheets.

Control:
The Homocysteine Control Kit is intended for use in quality control by monitoring accuracy and precision for the quantitative methods as specified in the value sheets.

Predicate devices

Roche claims substantial equivalence for the Homocysteine Enzymatic Reagent to the currently marketed Diazyme Homocysteine Enzymatic Assay cleared in K061296 and K042448.

Roche claims substantial equivalence for the Homocysteine Calibrator and Controls to the currently marketed Diazyme Homocysteine Calibrator and Controls cleared in K071971 and K042448, respectively.

Substantial equivalence - Reagent

The following table compares the features of the draft device with the predicate device for the reagent.

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Substantial equivalence – Reagent (continued)

Feature	Predicate Device: Diazyme Homocysteine Enzymatic Assay (K061296)	Draft Device: Homocysteine Enzymatic Assay
Intended Use	Assay is intended for the in vitro quantitative determination of total L-homocysteine in human serum or plasma. The reagents can assist in the diagnosis and treatment of patients suspected of having hyperhomocysteinemia and homocystinuria.	In vitro test for the quantitative determination of L-homocysteine in human serum and plasma on Roche/Hitachi **cobas c** systems. The assay can assist in the diagnosis of patients suspected of having hyperhomocysteinemia or homocystinuria.
Sample Types	Serum, Lithium Heparin, and EDTA	Serum, Lithium Heparin, K_2EDTA, and K_3EDTA
Instrument Platform	COBAS INTEGRA 400	**cobas c** 501
Calibrator	Homocysteine Calibrator, single level, diluted to form a 5-point calibration	same
Calibration Frequency	Each lot + interval (168 hours)	Every 7 days, after reagent lot change, and as required following quality control procedures
Calibration Mode	Logit/log5	RCM
Controls	Homocysteine Controls	same

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Substantial equivalence - Reagent (continued)

Feature	Predicate Device: Diazyme Homocysteine Enzymatic Assay (K061296)	Draft Device: Homocysteine Enzymatic Assay
Reagent Active Ingredients	R1: S-adenosylmethionine, TCEP, 2-oxoglutarate, NADH R2: homocysteine S-methyltransferase, glutamate dehydrogenase, casein (bovine) R3: adenosine deaminase (bovine), S-adenosyl-homocysteine hydrolase, casein (bovine)	same
Reagent Stability	Unopened: 2-8 °C until expiration date On-board in use: 60 days	Unopened: 2-8 °C until expiration date On-board in use: 4 weeks
Measuring Range	2.8 – 50 µmol/L	3 – 50 µmol/L
Lower Limits of Measure	LDL = 2.8 µmol/L	LoB = 3 µmol/L LoD = 3 µmol/L

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Substantial equivalence - Reagent (continued)

<table>
<tr><th>Feature</th><th>Predicate Device:
Diazyme Homocysteine
Enzymatic Assay (K061296)</th><th>Draft Device:
Homocysteine
Enzymatic Assay</th></tr>
<tr><td>Precision</td><td>
<table>
<tr><th></th><th>Value</th><th>CV Within Run</th><th>CV Total Precision</th></tr>
<tr><td>Hcy Low Control</td><td>7.0 µM</td><td>2.6%</td><td>2.7%</td></tr>
<tr><td>Hcy High Control</td><td>29.0 µM</td><td>2.3%</td><td>3.4%</td></tr>
<tr><td>Human serum 1</td><td>11.0 µM</td><td>2.5%</td><td>3.6%</td></tr>
<tr><td>Human serum 2</td><td>15.6 µM</td><td>1.9%</td><td>2.4%</td></tr>
</table>
</td><td>
<table>
<tr><th></th><th>Mean Value</th><th>CV Repeat-ability</th><th>CV Inter-mediate Precision</th></tr>
<tr><td>Hcy Control 1</td><td>12.2 µmol/L</td><td>1.5%</td><td>2.1%</td></tr>
<tr><td>Hcy Control 2</td><td>39.1 µmol/L</td><td>1.8%</td><td>2.0%</td></tr>
<tr><td>Human serum 1</td><td>8.26 µmol/L</td><td>2.0%</td><td>2.3%</td></tr>
<tr><td>Human serum 2</td><td>13.1 µmol/L</td><td>1.8%</td><td>2.1%</td></tr>
<tr><td>Human serum 3</td><td>30.0 µmol/L</td><td>1.4%</td><td>1.8%</td></tr>
<tr><td>Human serum 4</td><td>44.4 µmol/L</td><td>2.0%</td><td>2.2%</td></tr>
</table>
</td></tr>
<tr><td>Expected Values</td><td>US: 15 µmol/L is used as the cut-off value for normal levels of homocysteine in adults.

Europe: 12 µmol/L is used as the cut-off value for normal levels of homocysteine in adults.</td><td>same</td></tr>
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510(k) Summary, Continued

Substantial equivalence - Reagent (continued)

Feature	Predicate Device: Diazyme Homocysteine Enzymatic Assay (K061296)	Draft Device: Homocysteine Enzymatic Assay
Interferences	Patients who are taking methotrexate, carbamazepine, phenytoin, nitrous oxide, anticonvulsants, or 6-azuridine triacetate, may have higher levels of Hcy due to metabolic interference with Hcy metabolism S-Adenosylhomocysteine (SAH) will cause a significant positive interference. However, SAH is only detectable at sub-nmol/L concentrations in normal plasma, and should not cause concern. **Icterus**: No significant interference **Hemolysis**: No significant interference **Lipemia**: No significant interference	**NOTE: Patients who are taking methotrexate, carbamazepine, phenytoin, nitrous oxide, anticonvulsants, or 6-azuridine triacetate may have higher levels of Hcy due to metabolic interference with Hcy metabolism.** **S-Adenosylhomocysteine (SAH) will cause a significant positive interference. However, SAH is only detectable at sub-nmol/L concentrations in normal plasma, and should not cause concern.** **Icterus**: No significant interference up to an I index of 20 **Hemolysis**: No significant interference up to an H index of 100 **Lipemia**: No significant interference up to an L index of 250 **Triglycerides:** No significant interference up to 1790 mg/dl. **Drugs**: No interference was found at therapeutic concentrations using common drug panels.

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510(k) Summary, Continued

Substantial equivalence - Reagent (continued)

Feature	Predicate Device: Diazyme Homocysteine Enzymatic Assay (K061296)	Draft Device: Homocysteine Enzymatic Assay
Interferences, continued	**Other**: The following substances normally present in the serum produced less than 10% deviation when tested at the stated concentrations: 500 µM NH_4Cl, 1 mM NaPi, 1 mM NaF, 0.5 mM Glutathione, 10 mM Ascorbic Acid, 1 mM L-Cysteine, 20 µM S-Adenosylmethionine (SAM), 100 µM Adenosine, 100 µM Cystathionine Addition of 3-deazaadenosine to inhibit Hcy production in red cells has been suggested. However, the Homocysteine Enzymatic Assay can not use samples containing 3-deazaadenosine since it inhibits one of the key enzymes used in the assay.	Additional drugs tested include Glutathione at 0.5 mmol/L, Cystathionine at 100 µmol/L, and Pyruvate at 0.5 mmol/L; no interference was found. Addition of 3-deazaadenosine to inhibit Hcy production in red cells has been suggested. However, the Homocysteine Enzymatic Assay can not use samples containing 3-deazaadenosine since it inhibits one of the key enzymes used in the assay. In very rare cases, gammopathy, in particular IgM (Waldenstrom's macroglobulinemia), may cause unreliable results.

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Substantial equivalence - Calibrator

The following table compares the features of the draft device with the predicate device for the calibrator.

Feature	Predicate Device: Diazyme Homocysteine Calibrator (K071971)	Draft Device: Homocysteine Calibrator
Intended Use	The Diazyme Homocysteine Calibrator is intended for use in the calibration of quantitative determination of Homocysteine with the Diazyme Homocysteine Enzymatic methods on COBAS INTEGRA, **cobas c**, and Modular P analyzers.	The Homocysteine Calibrator Kit is intended for use in the calibration of quantitative Roche methods on Roche clinical chemistry analyzers as specified in the value sheets.
Analyte	Homocysteine	Same
Matrix	Human serum	Same
Storage	2-8 °C	Same

Substantial equivalence- Control Set

The following table compares the features of the draft device with the predicate device for the control set.

Feature	Predicate Device: Diazyme Homocysteine Controls (K042448)	Draft Device: Homocysteine Control
Intended Use	The Diazyme Homocysteine Controls are intended for use as part of a quality assurance system for the Diazyme Homocysteine Enzymatic Assay.	The Homocysteine Control Kit is intended for use in quality control by monitoring accuracy and precision for the quantitative methods as specified in the value sheets.
Analyte	Homocysteine	Same
Matrix	2 – level set with a normal serum homocysteine level and an abnormal homocysteine level	Same
Storage	2-8 °C	Same

End of Summary

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration

10903 New Hampshire Avenue
Silver Spring, MD 20993

Roche Diagnostics
c/o Susan Hollandbeck
9115 Hague Road
P. O. Box 50416
Indianapolis, IN 46250

JUN - 5 2012

Re: k113793
Trade Name: Homocysteine Enzymatic Assay; Homocysteine Calibrator Kit, Homocysteine Control Kit
Regulation Number: 21 CFR §862.1377
Regulation Name: Urinary Homocysteine (non quantitative) test system
Regulatory Class: Class II
Product Codes: LPS, JIX, JJX
Dated: May 23, 2012
Received: May 24, 2012

Dear Ms. Hollandbeck:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820).

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Office of In Vitro Diagnostic Device Evaluation and Safety at (301) 796-5450. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding postmarket surveillance, please contact CDRH's Office of Surveillance and Biometric's (OSB's) Division of Postmarket Surveillance at (301) 796-5760. For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance...

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-5680 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm

Sincerely yours,

Courtney H. Lias, Ph.D.
Director
Division of Chemistry and Toxicology Devices
Office of *In Vitro* Diagnostic Device
Evaluation and Safety
Center for Devices and Radiological Health

Enclosure

Indications for Use

510(k) Number (if known): K113793

Device Name: Homocysteine Enzymatic Assay; Homocysteine Calibrator Kit; and Homocysteine Control Kit

Indications For Use:

The Homocysteine Enzymatic Assay is an in vitro test for the quantitative determination of total L-homocysteine in human serum and plasma on Roche/Hitachi cobas c systems. The assay can assist in the diagnosis of patients suspected of having hyperhomocysteinemia or homocystinuria.

The Homocysteine Calibrator Kit is intended for use in the calibration of quantitative Roche methods on Roche clinical chemistry analyzers as specified in the value sheets.

The Homocysteine Control Kit is intended for use in quality control by monitoring accuracy and precision for the quantitative methods as specified in the value sheets.

Prescription Use ___X___ (Part 21 CFR 801 Subpart D) AND/OR Over-The-Counter Use _____ (21 CFR 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of In Vitro Diagnostic Devices (OIVD)

Division Sign-Off
Office of In Vitro Diagnostic Device
Evaluation and Safety

510(k) K113793